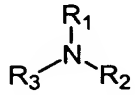
CLAIMS

What is claimed is:

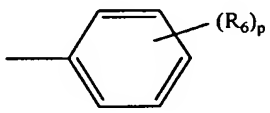
1. A method of modulating an Edg-3 receptor mediated biological activity comprising contacting a cell expressing the Edg-3 receptor with an amount of an modulator of the Edg-3 receptor sufficient to modulate the Edg-3 receptor mediated biological activity wherein compound of the structural formula (I):



(I)

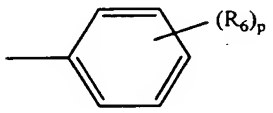
or a pharmaceutically available solvate or hydrate thereof, wherein;

each of R_1, R_2 and R_3 is independently -H, -halo, $-NO_2$, -CN, $-C(R_5)_3$, $-(CH_2)_mOH$, $-N(R_5)(R_5)$, $-O(CH_2)_mR_5$, $-C(O)R_5$, $-C(O)NR_5R_5$, $-C(O)NH(CH_2)_m(R_5)$, $-OCF_3$, -benzyl, $-CO_2CH(R_5)(R_5)$, $-(C_1\text{-}C_{10})$alkyl, $-(C_2\text{-}C_{10})$alkenyl, $-(C_2\text{-}C_{10})$alkynyl, $-(C_3\text{-}C_{10})$cycloalkyl, $-(C_8\text{-}C_{14})$bicycloalkyl, $-(C_5\text{-}C_{10})$cycloalkenyl, $-(C_5)$heteroaryl, $-(C_6)$heteroaryl, $-(C_5\text{-}C_{10})$heteroaryl, -naphthyl, $-(C_3\text{-}C_{10})$heterocycle, $-CO_2(CH_2)_mR_5$, -N(OH)aryl, $-NHC(O)R_5$, $-NHC(O)OR_5$, $-NHC(O)NHR_5$, -heterocylcoalkyl, $-C(S)N(R_5)(R_5)$, $-(C_1\text{-}C_{10})$alkylNHC(O)$(CH_2)_mR_5$, $-(C_1\text{-}C_{10})$alkylNR_5R_5, $-OC(O)(CH_2)_mCHR_5R_5$, $-CO_2(CH_2)_mCHR_5R_5$, $-OC(O)OR_5$, $-SR_5$, $-S(O)R_5$, $-S(O)_2R_5$, $-S(O)_2NHR_5$, or



R_3 is -H $-C(R_5)_3$, $-(CH_2)_mOH$, $-C(O)R_5$, $-C(O)NR_5R_5$, $-C(O)NH(CH_2)_m(R_5)$, -benzyl, $-CO_2CH(R_5)(R_5)$, $-(C_1\text{-}C_{10})$alkyl, $-(C_2\text{-}C_{10})$alkenyl, $-(C_2\text{-}C_{10})$alkynyl, $-(C_3\text{-}C_{10})$cycloalkyl, $-(C_8\text{-}C_{14})$bicycloalkyl, $-(C_5\text{-}C_{10})$cycloalkenyl, $-(C_5)$heteroaryl, $-(C_6)$heteroaryl, $-(C_5\text{-}C_{10})$heteroaryl, -naphthyl, $-(C_3\text{-}C_{10})$heterocycle, $-CO_2(CH_2)_mR_5$, -N(OH)aryl, $-NHC(O)R_5$, $-NHC(O)OR_5$, $-NHC(O)NHR_5$, -N=C(aryl), -heterocylcoalkyl, $-(C_1\text{-}C_{10})$alkylNHC(O)$(CH_2)_mR_5$, $-(C_1\text{-}C_{10})$alkylNR_5R_5,

$-OC(O)(CH_2)_mCHR_5R_5$, $-CO_2(CH_2)_mCHR_5R_5$, $-OC(O)OR_5$, $-SR_5$, $-S(O)R_5$, $-S(O)_2R_5$, $-S(O)_2NHR_5$, or



wherein;

each R_5 and R_6 is independently –H, -halo, $-NO_2$, -CN, -OH, $-CO_2H$, $-N(C_1-C_{10})alkyl(C_1-C_{10})alkyl$, $-O(C_1-C_{10})alkyl$, $-C(O)(C_1-C_{10})alkyl$, $-C(O)NH(CH_2)_m(C_1-C_{10})alkyl$, $-OCF_3$, -benzyl, $-CO_2(CH_2)_mCH((C_1-C_{10})alkyl(C_1-C_{10})alkyl)$, $-CO_2(C_1-C_{10})alkyl$, $-(C_1-C_{10})alkyl$, $-(C_2-C_{10})alkenyl$, $-(C_2-C_{10})alkynyl$, $-(C_3-C_{10})cycloalkyl$, $-(C_8-C_{14})bicycloalkyl$, $-(C_5-C_{10})cycloalkenyl$, $-(C_5)heteroaryl$, $-(C_6)heteroaryl$, -phenyl, naphthyl, $-(C_3-C_{10})heterocycle$, $-CO_2(CH_2)_m(C_1-C_{10})alkyl$, $-CO_2(CH_2)_mH$, $-NHC(O)(C_1-C_{10})alkyl$, $-NHC(O)NH(C_1-C_{10})alkyl$, -NH(aryl), -N=C(aryl), $-OC(O)O(C_1-C_{10})alkyl$, or $-SO_2NH_2$;

X is O, S, or $N(R_5)$;

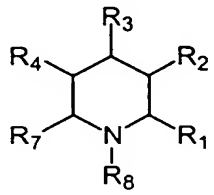
R_1, R_2 or R_3 taken in combination can form one or more substituted or unsubstituted 5 or 6 membered cyclic or heterocyclic rings or a 6-membered aromatic ring;

two R_6 groups on adjacent carbon atoms can together form a 5 or 6 membered cyclic or heterocyclic ring or a 6-membered aromatic ring;

each m is independently an integer ranging from 0 to 8; and

each p is independently an integer ranging from 0 to 5.

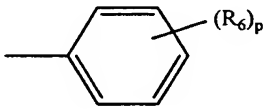
2. A method of modulating an Edg-2 receptor mediated biological activity in a subject comprising administering to the subject a therapeutically effective amount of a modulator of the Edg-2 receptor wherein the modulator a compound of the structural formula (II):



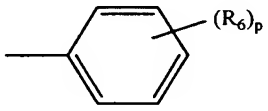
(II)

or a pharmaceutically available solvate or hydrate thereof, wherein;

each of R_1, R_2, R_3 R_4, R_7 and R_8 is independently -H, -halo, $-NO_2$, -CN, $-C(R_5)_3$, $-(CH_2)_mOH$, $-N(R_5)(R_5)$, $-O(CH_2)_mR_5$, $-C(O)R_5$, $-C(O)NR_5R_5$, $-C(O)NH(CH_2)_m(R_5)$, $-OCF_3$, -benzyl, $-CO_2CH(R_5)(R_5)$, $-(C_1-C_{10})$alkyl, $-(C_2-C_{10})$alkenyl, $-(C_2-C_{10})$alkynyl, $-(C_3-C_{10})$cycloalkyl, $-(C_8-C_{14})$bicycloalkyl, $-(C_5-C_{10})$cycloalkenyl, $-(C_5)$heteroaryl, $-(C_6)$heteroaryl, $-(C_5-C_{10})$heteroaryl, -naphthyl, $-(C_3-C_{10})$heterocycle, $-CO_2(CH_2)_mR_5$, -N(OH)aryl, $-NHC(O)R_5$, $-NHC(O)OR_5$, $-NHC(O)NHR_5$, -heterocylcoalkyl, $-C(S)N(R_5)(R_5)$, $-(C_1-C_{10})$alkylNHC(O)$(CH_2)_mR_5$, $-(C_1-C_{10})$alkylNR_5R_5, $-OC(O)(CH_2)_mCHR_5R_5$, $-CO_2(CH_2)_mCHR_5R_5$, $-OC(O)OR_5$, $-SR_5$, $-S(O)R_5$, $-S(O)_2R_5$, $-S(O)_2NHR_5$, or



R_3 is -H $-C(R_5)_3$, $-(CH_2)_mOH$, $-C(O)R_5$, $-C(O)NR_5R_5$, $-C(O)NH(CH_2)_m(R_5)$, -benzyl, $-CO_2CH(R_5)(R_5)$, $-(C_1-C_{10})$alkyl, $-(C_2-C_{10})$alkenyl, $-(C_2-C_{10})$alkynyl, $-(C_3-C_{10})$cycloalkyl, $-(C_8-C_{14})$bicycloalkyl, $-(C_5-C_{10})$cycloalkenyl, $-(C_5)$heteroaryl, $-(C_6)$heteroaryl, $-(C_5-C_{10})$heteroaryl, -naphthyl, $-(C_3-C_{10})$heterocycle, $-CO_2(CH_2)_mR_5$, -N(OH)aryl, $-NHC(O)R_5$, $-NHC(O)OR_5$, $-NHC(O)NHR_5$, -N=C(aryl), -heterocylcoalkyl, $-(C_1-C_{10})$alkylNHC(O)$(CH_2)_mR_5$, $-(C_1-C_{10})$alkylNR_5R_5, $-OC(O)(CH_2)_mCHR_5R_5$, $-CO_2(CH_2)_mCHR_5R_5$, $-OC(O)OR_5$, $-SR_5$, $-S(O)R_5$, $-S(O)_2R_5$, $-S(O)_2NHR_5$, or



wherein;

each R_5 and R_6 is independently –H, -halo, $-NO_2$, -CN, -OH, $-CO_2H$, $-N(C_1-C_{10})$alkyl(C_1-C_{10})alkyl, $-O(C_1-C_{10})$alkyl, $-C(O)(C_1-C_{10})$alkyl, $-C(O)NH(CH_2)_m(C_1-C_{10})$alkyl, $-OCF_3$, -benzyl, $-CO_2(CH_2)_mCH((C_1-C_{10})$alkyl$(C_1-C_{10})$alkyl), $-CO_2(C_1-C_{10})$alkyl, $-(C_1-C_{10})$alkyl, $-(C_2-C_{10})$alkenyl, $-(C_2-C_{10})$alkynyl,

-(C_3-C_{10})cycloalkyl, -(C_8-C_{14})bicycloalkyl, -(C_5-C_{10})cycloalkenyl, -(C_5)heteroaryl, -(C_6)heteroaryl, -phenyl, naphthyl, -(C_3-C_{10})heterocycle, -$CO_2(CH_2)_m$(C_1-C_{10})alkyl, -$CO_2(CH_2)_m$H, -NHC(O)(C_1-C_{10})alkyl, -NHC(O)NH(C_1-C_{10})alkyl, -NH(aryl), -N=C(aryl), -OC(O)O(C_1-C_{10})alkyl, or -SO_2NH_2;

X is O, S, or N(R_5);

R_1 and R_2, R_2 and R_3, R_3 and R_4, R_4 and R_7, or R_7 and R_8 taken in combination can form one or more substituted or unsubstituted 5 or 6 membered cyclic or heterocyclic rings or a 6-membered aromatic ring;

two R_6 groups on adjacent carbon atoms can together form a 5 or 6 membered cyclic or heterocyclic ring or a 6-membered aromatic ring;

each m is independently an integer ranging from 0 to 8; and

each p is independently an integer ranging from 0 to 5.

3. The method of Claim 1 or 2, wherein the modulator is an agonist.

4. The method of Claim 1 or 2, wherein the modulator is an antagonist.

5. The method of Claim 1 or 2, wherein the modulator exhibits at least about 200 fold inhibitory selectivity for Edg-2 relative to other Edg receptors.

6. The method of Claim 1 or 2, wherein the modulator exhibits at least about 40 fold inhibitory selectivity for Edg-2 relative to other Edg receptors.

7. The method of Claim 1 or 2, wherein the modulator exhibits at least about 12 fold inhibitory selectivity for Edg-2 relative to other Edg receptors.

8. The method of Claim 1 or 2, wherein the modulator exhibits at least about 5 fold inhibitory selectivity for Edg-2 relative to other Edg receptors.

9. The method of Claim 1 or 2, wherein the modulator exhibits at least about 20 fold inhibitory selectivity for Edg-2 relative to other Edg receptors.

10. The method of Claim 1 or 2, wherein the modulator exhibits at least about 200 fold inhibitory selectivity for Edg-2 relative to Edg-4 and Edg-7 receptors.

11. The method of Claim 1 or 2, wherein the modulator exhibits at least about 40 fold inhibitory selectivity for Edg-2 relative to Edg-4 and Edg-7 receptors.

12. The method of Claim 1 or 2, wherein the modulator exhibits at least about 12 fold inhibitory selectivity for Edg-2 relative to Edg-4 and Edg-7 receptors.

13. The method of Claim 1 or 2, wherein the modulator exhibits at least about 5 fold inhibitory selectivity for Edg-2 relative to Edg-4 and Edg-7 receptors.

14. The method of Claim 1 or 2, wherein the biological activity is cell proliferation.

15. The method of Claim 14, wherein the modulator exhibits at least about 200 fold inhibitory selectivity for Edg-2 relative to other Edg receptors.

16. The method of Claim 14, wherein the modulator exhibits at least about 5 fold inhibitory selectivity for Edg-2 relative to other Edg receptors.

17. The method of Claim 14, wherein the modulator exhibits at least about 200 fold inhibitory selectivity for Edg-2 relative to Edg-4 and Edg-7 receptors.

18. The method of Claim 14, wherein the modulator exhibits at least about 5 fold inhibitory selectivity for Edg-2 relative to Edg-4 and Edg-7 receptors.

19. The method of Claim 14, wherein cell proliferation leads to ovarian cancer, peritoneal cancer, endometrial cancer, cervical cancer, breast cancer, colon cancer or prostrate cancer.

20. The method of Claim 14, wherein cell proliferation is stimulated by LPA.

21. The method of Claim 1 or 2, wherein the biological activity is calcium mobilization, VEGF synthesis, IL-8 synthesis, platelet activation, cell migration,

phosphoinositide hydrolysis, inhibition of cAMP formation, actin polymerization, apoptosis, angiogenesis, inhibition of wound healing, inflammation, cancer invasiveness, supressing autoimmune responses, or atherogenesis.

22. The method of Claim 1 or 2 wherein the modulator binds to the Edg-2 receptor with a binding constant of at least about 10 nm.

23. The method of Claim 1 or 2 wherein the modulator binds to the Edg-2 receptor with a binding constant between about 1 μM and 100 fM.

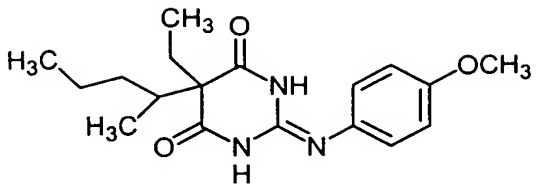
24. The method of Claim 1 or 2, wherein the modulator is a nucleic acid, protein or carbohydrate.

25. The method of Claim 1 or 2, wherein the modulator is an organic molecule of molecular weight of less than 750 daltons.

26. The method of Claim 1, wherein the cell is a hepatoma cell, an ovarian cell, an epithelial cell, a fibroblast cell, a neuronal cell, a carcinoma cell, a pheochromocytoma cell, a myoblast cell, a platelet cell or a fibrosarcoma cell.

27. The method of Claim 21, wherein the cell is OV202 human ovarian cell, a HTC rat hepatoma cell, a CAOV-3 human ovarian cancer cell, MDA-MB-453 breast cancer cell, MDA-MB-231 breast cancer cell, HUVEC cells A431 human epitheloid carcinoma cell or a HT-1080 human fibrosarcoma cell.

28. The method of Claim 25 wherein the modulator has the following structural formula:



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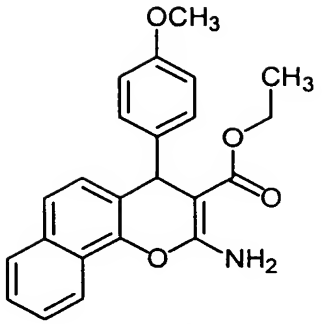

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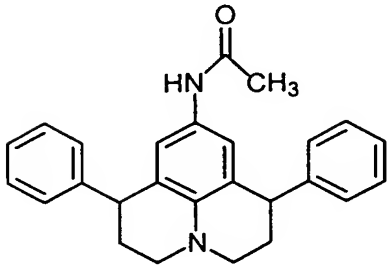

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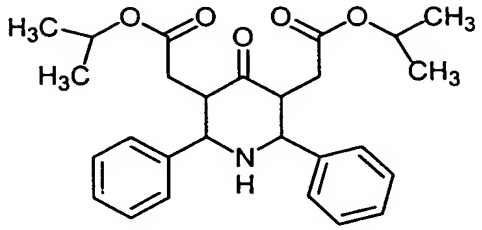

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29. A method for treating or preventing cancers, acute lung diseases, acute inflammatory exacerbation of chronic lung diseases, surface epithelial cell injury, or cardiovascular diseases in a patient comprising administering to a patient in need of such treatment or prevention a therapeutically effective amount of a compound of structural formula (I) or (II).

30. A method for treating or preventing ovarian cancer, peritoneal cancer, endometrial cancer, cervical cancer, breast cancer, colorectal cancer, uterine cancer, stomach cancer, small intestine cancer, thyroid cancer, lung cancer, kidney cancer, pancreas cancer, prostrate cancer, adult respiratory distress syndrome (ARDS), asthma, transcorneal freezing, cutaneous burns, ischemia or arthesclerosis in a patient comprising administering to a patient in need of such treatment or prevention a therapeutically effective amount of a compound of structural formula (I) or (II).

31. A method for treating or preventing cancers, acute lung diseases, acute inflammatory exacerbation of chronic lung diseases, surface epithelial cell injury, or cardiovascular diseases in a patient comprising administering to a patient in need of

such treatment or prevention a therapeutically effective amount of a compound of structural formula (I) or (II) and one or more agonists or antagonists of an Edg-2 receptor.

32. A method for treating or preventing cancers, acute lung diseases, acute inflammatory exacerbation of chronic lung diseases, surface epithelial cell injury, or cardiovascular diseases in a patient comprising administering to a patient in need of such treatment or prevention a therapeutically effective amount of a compound of structural formula (I) or (II) and one or more drugs useful in treating or preventing cancers, acute lung diseases, acute inflammatory exacerbation of chronic lung diseases, surface epithelial cell injury, or cardiovascular diseases.